Stereocontrol in the Peterson Olefination of Ketones

Natalia Ya. Grigorieva,* Ol'ga A. Pinsker and Alexander M. Moiseenkov

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation. Fax: +7 095 135 5328

A highly stereoselective method for the olefination of ketones with alkyl trialkylsilylacetates is described.

The Peterson olefination of carbonyl compounds is one of the most useful methods of carbon chain elongation.[1] However, under conditions suitable for converting aldehydes into products with *E*- or *Z*-stereoselectivity of up to 95–98% (see refs. 2 and 3, respectively), a rather low (60–65%) stereoselectivity is usually observed for ketones (for exceptions, see ref. 4).

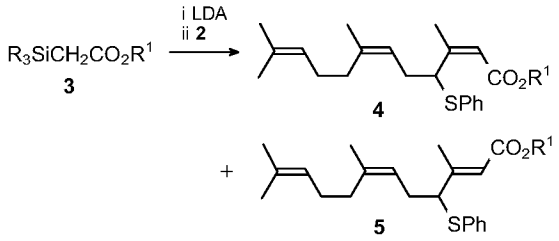
Here we describe an approach which has enabled us to perform the Peterson olefination of isoprenoid ketones with up to 90% *Z*-stereoselectivity. It is based on an assumption that the differences in stereochemical outcome of the Peterson olefination of aldehydes and ketones are due to steric factors. Namely, the steric non-equivalence of H and CH_2 groups connected with the carbonyl function in aldehydes ensures the high stereoselectivity of their olefination, while nearly identical steric parameters of the corresponding groups in ketones result in low stereoselection.

This reasoning prompted us to study the possibility of increasing the *Z*-stereoselectivity of the olefination of isoprenoid ketones by introducing an auxiliary and bulky substituent (*e.g.*, PhS) at the C^3-position of the isoprenoid methyl ketone, which could be easily removed from the reaction products.

Under the conditions given in Scheme 1, it was possible to convert nerylacetone **1** into 3-phenylthioketone **2**† (isolated yield 60%). Olefination of **2** with ethyl trimethylsilylacetate **3** (R = Me, R^1 = Et) (Table 1) deprotonated by lithium diisopropylamide (LDA) furnished a 88:12 mixture of esters **4** and **5** (^{1}H NMR and HPLC data).†

Variations in the size of the substituents R and R^1 in the Peterson reagent affect significantly the selectivity of the olefination (see Table 1). Thus, the highest selectivity (up to 90% of *Z*-isomer) is observed when R = R^1 = Me. Contrary to the known data,[3,4c] an increase in the size of the substituent R at the silicon atom only results in a slight decrease in *Z*/*E* ratio (compare entries 2, 4 and 6 and also 3 and 5 in Table 1). At the same time, the use of **3** containing a bulky R^1 group, such as Bu^t, results in a decrease in the stereoselectivity, and entries 7 and 8 (Table 1) show that the reaction becomes virtually non-selective.

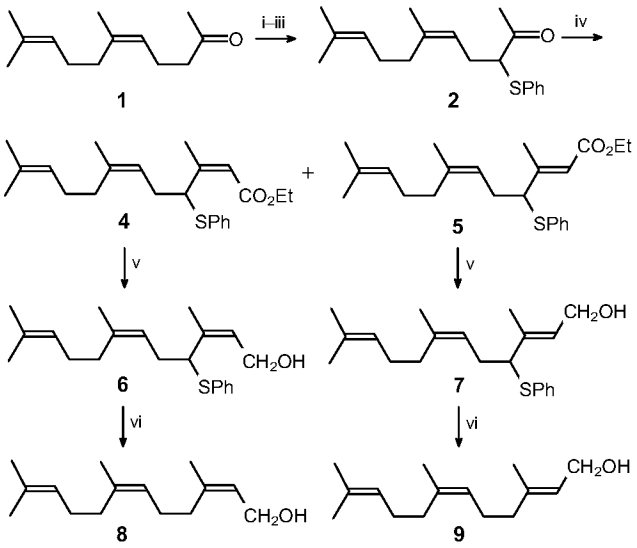
Table 1 The effect of substituents R and R^1 in alkyl silylacetates **3** on the stereochemistry of olefination of ketone **2**.



Entry	R_3	R^1	Yield (%)	Ratio **4**/**5**
1	Me_3	Me	78	90:10
2	Me_3	Et	70	88:12
3	Me_3	Bu^t	70	80:20
4	Me_2Ph	Et	90	85:15
5	Me_2Ph	Bu^t	60	80:20
6	$MePh_2$	Et	65	80:20
7	$MePh_2$	Bu^t	40	55:45
8	Ph_3	Bu^t	8	55:45

Ethyl esters **4** and **5**, as well as their methyl and *tert*-butyl analogues, are quantitatively separated by flash chromatography and smoothly transformed to *Z,Z*- **8** and *E,Z*-farnesol **9** *via* 4-phenylthiocarbinols **6** and **7**, respectively (Scheme 1).

Investigations into the stereochemical aspects of other reactions of **2** and related ketones are currently in progress.



Scheme 1 *Reagents and conditions*: i, $(Me_3Si)_2NNa/Et_2O$–THF (1:1, v/v), 20 °C, 2.5 h; ii, $(PhS)_2$/THF–HMPA (3:1, v/v), −5 ± 2 °C, 1 h; iii, flash chromatography on SiO_2 (from hexane to benzene); iv, $Me_3SiCHCOOEt$/THF, −70 °C, 2 h → 20 °C, 2 h; v, AlH_3/Et_2O, −10 °C, 2 h; vi, Na/NH_3–Et_2O (5:1, v/v), dibenzo-18-crown-6, −70 °C, 1 h.

† All new compounds **2** and **4**–**7** gave satisfactory analytical and spectroscopic data. ^{1}H NMR data (250 MHz, $CDCl_3$; *J* values are given in Hz) for **2**: δ 1.65 (3H, s, *cis*-Me), 1.72 and 1.74 (3H and 3H, 2s, *trans*-Me), 2.07 (4H, br.s, H-7 and H-8), 2.27 (3H, s, MeCO), 2.50 (2H, m, H-4), 3.65 (1H, t, *J* = 7.5, H-3), 5.15 (2H, m, H-5 and H-9), 7.35 (5H, m, Ph); for **4**: δ 1.2 (3H, t, *J* = 7, Me), 1.62 (3H, br.s, *cis*-Me), 1.7 (6H, br.s, *trans*-Me), 1.92 (3H, d, *J* = 1.5, Me-3), 2.06 (4H, m, CH_2C=C), 2.45 (2H, m, H-5), 4.02 (2H, q, *J* = 7, CH_2O), 5.12 (2H, m, H-6 and H-10), 5.62 (1H, br.s, H-2), 5.65 (1H, t, *J* = 7, H-4), 7.3 (5H, m, Ph); for **5**: δ 1.25 (3H, t, *J* = 7, Me), 1.62 (3H, br.s, *cis*-Me), 1.71 (6H, br.s, *trans*-Me), 2.06 (4H, m, CH_2C=C), 2.2 (3H, d, *J* = 1.5, Me-3), 2.42 (2H, m, H-5), 3.56 (1H, t, *J* = 7, H-4), 4.08 (2H, q, *J* = 7, CH_2O), 5.1 (2H, m, H-6 and H-10), 5.45 (1H, br.s, H-2), 7.3 (5H, m, Ph). ^{13}C NMR data (75.5 MHz, $CDCl_3$) for **2**: δ 17.7 (*cis*-Me-10), 23.4 (Me-6), 25.7 (*trans*-Me-10), 26.4 (4), 26.9 (8), 28.9 (CH_3CO), 32.2 (7), 57.9 (3), 120.4(5), 124.0 (9), 132.1 (10), 138.7 (6), 205.2 (2); for **4**: δ 14.3 (CH_3CH_2), 17.7 (*cis*-Me-11), 19.4 (Me-3), 23.4 (Me-7), 25.7 (*trans*-Me-11), 26.5 (9), 30.9 (5), 32.2 (8), 47.7 (4), 59.6 (CH_2O), 119.0 (2), 121.1 (6), 124.2 (10), 132.1 (11), 137.7 (7), 156.6 (3), 165.8 (1); for **5**: δ 14.3 (CH_3CH_2), 15.1 (Me-3), 17.7 (*cis*-Me-11), 23.4 (Me-7), 25.4 (*trans*-Me-11), 26.9 (9), 31.0 (5), 32.2 (8), 59.1 (4), 59.7 (CH_2O), 117.6 (2), 120.9 (6), 124.0 (10), 133.2 (11), 138.1 (7), 156.6 (3), 166.3 (1).

References

1 (*a*) D. J. Ager, *Synthesis*, 1984, 384; (*b*) D. J. Ager, *Org. React.*, 1990, **38**, 1.

2 S. Kanemasa, J. Tanaka, H. Nagahama and O. Tsuge, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 3385 and references cited therein.

3 (*a*) Y. Yamakado, M. Ishiguro, N. Ikeda and H. Yamamoto, *J. Am. Chem. Soc.*, 1981, **103**, 5568; (*b*) A. R. Bassindale, R. J. Ellis and P. G. Taylor, *Tetrahedron Lett.*, 1984, **25**, 2705 and references cited therein.

4 (*a*) M. Larcheveque, Ch. Legueut, A. Debal and J. Y. Lallemand, *Tetrahedron Lett.*, 1981, **22**, 1595; (*b*) M. Visnick, L. Strekowski and M. A. Battiste, *Synthesis*, 1983, 284; (c) L. Strekowski, M. Visnick, and M. A. Battiste, *Tetrahedron Lett.*, 1984, **25**, 5603; (*d*) I. Černy, V. Pouzar, P. Drašar, F. Tureček and M. Havel, *Collect. Czech. Chem. Commun.*, 1986, **51**, 128.

Received: Moscow, 8th April 1994
Cambridge, 10th May 1994; Com. 4/02262I